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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference YCT-770	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP02/13858	International filing date (*day/month/year*) 27 December 2002 (27.12.02)	Priority date (*day/month/year*) 28 December 2001 (28.12.01)
International Patent Classification (IPC) or national classification and IPC A61K 38/40, 38/16, 9/14, 9/16, 9/20, 9/48, A61P 1/16, 3/04, 3/06, 3/10, 9/12		
Applicant NRL PHARMA, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 20 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 19 February 2003 (19.02.03)	Date of completion of this report 24 September 2003 (24.09.2003)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP02/13858

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:

pages 2-4, 16, 21, as originally filed
pages _____, filed with the demand
pages 1, 5-15, 17-20, filed with the letter of 05 September 2003 (05.09.2003)

☒ the claims:

pages 4-7, 12-16, 20-26, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages 1-3, 8-11, 17-19, filed with the letter of 05 September 2003 (05.09.2003)

☒ the drawings:

pages 1/14-14/14, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP02/13858

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 17-26

because:

☒ the said international application, or the said claims Nos. 17-26 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See supplemental sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 17-26 .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1

Claims 17-26 relate to methods for the treatment of the human body by therapy, and therefore relate to a subject matter for which this International Preliminary Examining Authority is not required to conduct an international preliminary examination under the provisions of PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1, 3-6, 8, 9, 11-14, 16	YES
	Claims	2, 7, 10, 15	NO
Inventive step (IS)	Claims	1, 3, 9, 11	YES
	Claims	2, 4-8, 10, 12-16	NO
Industrial applicability (IA)	Claims	1-16	YES
	Claims		NO

2. Citations and explanations

Document 1: JP 2000-325046 A (Meiji Milk Products Co., Ltd.), 28 November 2000

Document 2: JP 2001-048808 A (Morinaga Milk Industry Co., Ltd.), 20 February 2001

Document 3: WO 00/22909 A2 (Biotech Australia Pty. Ltd.), 27 April 2000

Document 4: WO 91/04015 A1 (Bukh Meditec A/S), 04 April 1991

Document 5: WO 98/44940 A1 (Agennix, Inc.), 15 October 1998

Document 6: EP 955058 A1 (Morinaga Milk Industry Co., Ltd.), 10 November 1999

Document 1 cited in the international search report discloses agents for the prevention and treatment of liver disease, which have lactoferrin as the active ingredient (refer to claim 1), and discloses the application of these agents in relation to hepatic steatosis (refer to paragraph [0011]).

Document 2 cited in the international search report discloses a method for producing an enteric sugar-coated tablet, which includes a step wherein lactoferrin is mixed with other components in a dried state and thereafter is formed into a tablet (refer to column 11, example 3).

Document 3 cited in the international search report discloses the feature of coating a biologically active component with an enteric coating so that the proteolysis of the component in the stomach is inhibited and the component is taken up from the intestines (refer to the abstract), and also indicates that lactoferrin can be used as said biologically active component (refer to claim 32).

Document 4 cited in the international search report discloses a composition that is provided with an enteric coating (refer to claim 45), a feature wherein lactoferrin can be used as a medicinal drug (refer to page 15, line 20) and a feature wherein a medicinal drug can be coated with an enteric coating in cases when it is preferable that the medicinal drug not be proteolyzed by stomach acid (refer to page 27, lines 23-29).

Document 5 cited in the international search report discloses a feature wherein lactoferrin can be coated with an enteric coating (refer to page 17, lines 16-17).

Document 6 cited in the international search report discloses a method for producing lactoferrin tablets by mixing lactoferrin with other components in a dried state and thereafter forming tablets (refer to the test and the examples).

Claims 2, 7, 10 and 15

Document 1 discloses the feature of using lactoferrin for the treatment of hepatic steatosis; therefore, the inventions set forth in claims 2, 7, 10 and 15 lack novelty and do not involve an inventive step in the light of document 1.

Furthermore, in the response to the written opinion dated 05 September 2003, the applicant asserts that document 1 merely mentions the application of applying lactoferrin in relation to hepatic steatosis, but does not present data related thereto; thus, due to the complex

etiology of hepatic steatosis, there is scant logical basis to assume that it is possible to apply lactoferrin to all forms of hepatic steatosis simply because it has a hepatopathy-inhibiting action. Therefore, the inventions set forth in this application are novel and involve an inventive step.

However, document 1 indicates that lactoferrin exhibits a hepatopathy-inhibiting action and a TNFα production-inhibiting action, and the fact that lactoferrin has such actions is considered to constitute a logical basis for the possibility of applying lactoferrin in relation to hepatic steatosis, which is a cause of decreased liver functions.

In addition, the inventions set forth in claims 2, 7, 10 and 15 of this application naturally include compositions for treating hepatic steatosis, which is a cause of decreased liver functions; thus, the inventions set forth in the abovementioned claims of this application are not considered to be different from the inventions disclosed in document 1 with regards to this feature. Therefore, the abovementioned assertions by the applicant cannot be accepted.

Claims 4, 8, 12 and 16

The inventions set forth in claims 4, 8, 12 and 16 are not disclosed in documents 1-6; therefore, they are novel.

However, the technical feature of producing tablets by mixing lactoferrin with other components in a dried state and thereafter forming tablets is well known as disclosed in documents 2 and 6; therefore, it is thought that a person skilled in the art could apply this production method in the invention disclosed in document 1 as necessary.

In addition, there are not considered to be any

significant effects that result from this feature.

Therefore, the inventions set forth in claims 4, 8, 12 and 16 do not involve an inventive step in the light of documents 1, 2 and 6.

Claims 5, 6, 13 and 14

The inventions set forth in claims 5, 6, 13 and 14 are not disclosed in documents 1-6; therefore, they are novel.

However, it is conventional to coat an enteric coating upon medicinal drugs that comprise lactoferrin as an active ingredient, as disclosed in documents 2-5. Thus, it is thought that a person skilled in the art could coat the invention disclosed in document 1 with an enteric coating as necessary.

In addition, there are not considered to be any significant effects that result from this feature.

Therefore, the inventions set forth in claims 5, 6, 13 and 14 do not involve an inventive step in the light of documents 1-5.

Claims 1, 3, 9 and 11

The inventions set forth in claims 1, 3, 9 and 11 are not disclosed or suggested in documents 1-6; therefore, they are novel and involve an inventive step.